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ORIGINAL ARTICLE

Experience of the national cohort of pregnant women with HIV and their children in Spain: temporal trends in vertical transmission of HIV and associated infections☆

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KEYWORDS
HIV;
Mother-to-child transmission;
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Abstract
Introduction: The vertical transmission rate (VTR) of HIV has decreased to less than 2% in high-income countries, in spite of which perinatal infections continue to occur. We present data from the national cohort of pregnant women living with HIV and their children in Spain. The objectives were to describe the characteristics of this population, evaluate the VTR of HIV, the safety of antiretroviral therapy (ART) and the prevalence of coinfection.

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Patients and methods: Multicentre prospective, observational and descriptive study with participation of 62 hospitals. The sample included pegnant women living with HIV whose children were born between January 2020 and December 2022. We collected prospective data on the characteristics of mothers and children using an online questionnaire (REDCap web application).
Results: The study included 414 mother-child dyads. Most mothers were immigrants (227/349; 65.1%). The main route of HIV infection was heterosexual transmission (160/402; 39.8%), followed by vertical transmission (44/402; 10.9%). The diagnosis was made before conception in 313/389 women (80.4%), 394/402 (98%) received ART during pregnancy and 356/402 (89.3%) had an undetectable viral load at the time of delivery. The delivery was vaginal in 230/388 children (59.3%). The proportion of preterm birth was 11.1%. The most frequent neonatal prophylaxis approach was monotherapy with zidovudine (358/414; 86.5%). There were 3 cases of vertical transmission of HIV (95% CI, 0%–1.54%). Only one newborn was breastfed.
Conclusions: At present, most women living with HIV in Spain receive the diagnosis before conception, are of foreign ancestry and achieve good control of the infection. Although the VTR is very low in Spain, there are still infections that could be prevented with early diagnosis and treatment.

PALABRAS CLAVE
VIH;
Transmisión vertical;
Infección perinatal;
Tratamiento antirretroviral

Experiencia de la cohorte nacional de mujeres embarazadas que viven con vih y sus hijos en España: evolución de la transmisión materno-infantil de VIH e infecciones asociadas

Resumen
Introducción: La tasa de transmisión materno-infantil (TMI) del VIH ha disminuido a menos del 2% en países desarrollados, a pesar de lo cual siguen produciéndose infecciones. Se presentan los datos de la Cohorte Nacional Española de mujeres embarazadas que viven con VIH y sus hijos. Los objetivos fueron describir sus características, evaluar la TMI de VIH, la seguridad del tratamiento antirretroviral (TAR) y la prevalencia de coinfecciones.
Pacientes y métodos: Estudio descriptivo, observacional, prospectivo y multicéntrico con participación de 62 hospitales. Se incluyeron las embarazadas cuyos hijos nacieron entre enero 2020 y diciembre 2022. Se recogieron prospectivamente características de las madres y niños en REDCap.
Resultados: Hubo 414 pares madre-niño. Las madres fueron migrantes 227/349 (65,1%). La principal vía de adquisición del VIH fue la heterosexual (160/402; 39,8%), seguido de la TMI (44/402; 10,9%). En 313/389 (80,4%) el diagnóstico fue previo al embarazo, 394/402 (98%) recibieron TAR durante la gestación y 356/402 (89,3%) presentaba carga viral indetectable al parto. Hubo 230/388 (59,3%) neonatos nacidos por parto vaginal. La tasa de prematuridad fue 11,1%. La profilaxis neonatal más empleada (358/414; 86,5%) fue monoterapia con zidovudina. Hubo 3 casos de TMI del VIH (0,72% (IC 95%; 0%–1,54%), todos ellos con infección intraútero. Todos menos 1 recibieron lactancia artificial.
Conclusiones: Actualmente las mujeres que viven con VIH en nuestro medio son migrantes, diagnosticadas mayoritariamente antes de la gestación, y logran adecuada situación inmunovirológica. Aunque la tasa de TMI es muy baja en nuestro país continúan ocurriendo infecciones prevenibles con diagnóstico y tratamiento más precoces.

Introduction

Vertical transmission (VT) continues to be the leading route of transmission of human immunodeficiency virus (HIV) in paediatric patients. In recent decades, while HIV vertical transmission prevention protocols have succeeded in reducing the incidence of new infections through this route to less than 2% in developed countries,[1,2] there are still infections that could be prevented.[3] Therefore, the detection of any new cases of HIV infection in children born in Spain is essential in order to identify missed opportunities in prevention and implement strategies to improve this aspect.

On the other hand, as has become evident throughout the epidemic, antiretroviral therapy (ART) during pregnancy is

not free of toxicity for either mother or newborn, and some of its side effects in the short, medium and long term remain unknown.[4] This explains the importance of obtaining data from large cohorts of mother-child dyads that can allow an understanding of the course of vertically transmitted infections and the adverse effects of ART on pregnant women and their offspring. There is also a dearth of information on the prevalence of coinfection in this subset of women, for instance with hepatitis B virus (HBV), hepatitis C virus (HCV) or syphilis, so accurate data on the prevalence of VT of these infections is not currently available.[5,6]

With the aim of collecting data on the VT of HIV in Spain, the National Cohort of Pregnant Women Living with HIV and their Exposed Children in Spain was instituted in 2020. The primary objectives of establishing this cohort were to describe the current characteristics of pregnant women living with HIV and their offspring and assess epidemiological trends in the VT of HIV, the ART used in pregnant women and its potential adverse effects and the prevalence of coinfection in this population.

Patients and methods

The previous experience of the Madrid cohort of pairs of mothers living with VIH and their exposed offspring, with participation of 9 public hospitals in the Community of Madrid and a duration of follow-up of 20 years[7] guided the design of a multicentre study in a nationwide cohort of pregnant women living with HIV and their newborn infants. After receiving the approval of the Clinical Research Ethics Committee (CREC) of each participating centre (including the CREC of Hospital Clínico San Carlos as the coordinating centre [ruling 21/272-E] and the CREC of the CoRISpe [ruling 14/429-E]), and with the support for the project of the Asociación Española de Pediatría (AEP, Spanish Association of Pediatrics) and the Ministry of Health, the working group developed a questionnaire using the Research Electronic Data Capture (REDCap) platform, hosted at the Instituto de Investigación Sanitaria Gregorio Marañón (IISGM). The following steps were recruiting the participating centres and obtaining the confidentiality agreement forms in which researchers in each centre agreed to uphold confidentiality and personal data protection. The health records of mothers and children were anonymised by means of codes that precluded the identification of the patient. The competent CREC approved the study protocol and the waiver of signed informed consent (CREC ruling 21/272-E of 30/04/2021) and authorised the retrospective collection of data for births that had taken place between January 1, 2020 and March 31, 2021 and prospective collection of data for births that took place from April 1, 2021.

Once this was done, a multicentre prospective observational and descriptive study was initiated with the participation of 62 public and private hospitals in 16 autonomous communities in Spain, distributed throughout the entire national territory with the exception of Navarre and Catalonia.

The study includes data for pregnant women living with HIV (diagnosed before conception, during gestation or during delivery or in the immediate postpartum period) whose offspring were born on or after January 1, 2020. We collected prospective data on demographic characteristics, HIV infection-related variables (including the plasma viral load [PVL] and CD4 count results obtained in the last prenatal care visit), the ART regimen used before and during pregnancy and the potential adverse effects associated with it, substance use, coinfection by HBV, HCV or syphilis and type of delivery. When it came to the newborn infant, the collected data included the gestational age, sex, anthropometric measurements at birth, congenital anomalies, infant feeding modality and regimen and duration of neonatal antiretroviral prophylaxis. We also collected the results of the HIV polymerase chain reaction (PCR) test conducted within 48 h of birth and starting from 3 months post birth, the results of HIV antibody/antigen tests from age 12 months and data on the VT of HBV, HCV and syphilis.

We defined adequate prenatal care as the mother attending at least one prenatal care visit per trimester.

We defined in utero transmission as a positive HIV PCR test result in the infant within 48 h of birth and intrapartum transmission as a negative result before 48 h followed by a positive PCR or antibody/antigen test for HIV from age 18 months.

At regular intervals, reminders were sent to the researchers in each centre to make the pertinent notifications of the identified congenital anomalies to the Agencia Española de Medicamentos and Productos Sanitarios (AEMPS, Spanish Agency of Medicines and Medical Products).

The statistical analysis was carried out with the software package Statistical Package for the Social Sciences (SPSS), version 26.0. We summarised qualitative variables as frequency distributions. Quantitative variables were expressed as mean and standard deviation. Continuous variables that did not follow a normal distribution were expressed as median and interquartile range (IQR). For normally distributed quantitative data, we used analysis of variance (ANOVA) and for those that did not follow a normal distribution, the nonparametric Kruskal-Wallis test.

Results

The sample included a total of 414 mother-child dyads (402 women, 12 twin pregnancies) recruited between January 1, 2020 and December 31, 2022 (with a minimum duration of follow-up for the infants of 6 weeks). Of all the mothers, 122/349 (34.9%) were not immigrants, defined as born in Spain, and 227/349 (65.1%) were immigrants. For 186/402 of the mothers (46.2%), the route by which they had become infected by HIV was not documented, while heterosexual transmission was documented in 160/402 (39.8%) and VT in 44/402 (10.9%) (Table 1).

In 313/389 of the mothers (80.4%), the diagnosis of HIV infection was made before the current pregnancy, in 75/389 (19.5%) during pregnancy and in 1/389 (0.25%) at the time of delivery. Prenatal care was adequate in 358/402 (89%) of the women. When it came to ART, 394/402 (98%) received it during pregnancy. In 133/402 (33.1%), the regimen was modified during pregnancy and 88/402 (21.8%) started ART during pregnancy. Table 2 presents the most frequent ART regimens.

The analysis of the immune status and HIV control in mothers during the last prenatal checkup showed that

Table 1 Epidemiological and clinical characteristics of pregnant women living with HIV in Spain.

Characteristics	n/N (%)
Age (years)	
Median (IQR)	32.9 (28.7−37.7)
Place of birth, n (%)	
Non-immigrant (Spain)	122/349 (34.9%)
Sub-Saharan Africa	111/349 (31.8%)
Latin America	82/349 (23.5%)
Eastern Europe	19/349 (5.4%)
Asia	3/349 (0.8%)
Other	12/349 (3.4%)
Route of HIV transmission in mother	
Sexual	160/402 (39.8%)
Perinatal	44/402 (10.9%)
Intravenous drug use	2/402 (0.5%)
Transfusion	3/402 (0.7%)
Coinfections	
HBV	
Past infection	18/402 (4.5%)
Active infection	9/402 (2.2%)
HCV	
Treated, sustained virologic response	13/402 (3.4%)
Untreated	5/402 (1.2%)
Syphilis	6/402 (1.5%)
Substance use	
Tobacco	55/402 (13.2)
Alcohol	15/402 (3.6)

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range.

Table 2 Antiretroviral therapy in pregnant women living with HIV in Spain.

Characteristics of ART	n/N (%)
ART at some point during gestation	394/402 (98%)
ART before gestation	314/402 (78.1%)
Continued with same ART regimen	181/402 (45%)
Change in ART regimen	133/402 (33.1%)
Most frequent modified ART regimens	
TDF/FTC/RAL	212/402 (52.7%)
ABC/3TC/RAL	52/402 (12.9%)
TDF/FTC/DTG	25/402 (6.4%)
ABC/3TC/DTG	22/402 (5.5%)
TDF/FTC/DRV	18/402 (4.6%)
Other	73/402 (18.1%)
Started ART during pregnancy	88/402 (21.9%)
Timing of ART initiation	
1st trimester	177/398 (44%)
2nd trimester	177/398 (44%)
3rd trimester	44/398 (11%)
Main ART initiation regimens	
TDF/FTC/RAL	252/402 (62.6%)
TDF/FTC/DTG	59/402 (14.6%)
Other	91/402 (22.6%)

ART, antiretroviral therapy; HIV, human immunodeficiency virus; 3TC, lamivudine.

Table 3 Congenital anomalies described in children of mothers living with HIV in Spain.

Congenital anomalies	n/N (%)
	18/414 (4.3%)
Cardiac	5/414 (1.2%)
Membranous VSD	
Right-sided aortic arch with ALSA	
Right ventricular hypertrophy	
Foramen oval permeable	
ARSA	
Renal	4/414 (0.9%)
Horseshoe kidney	
Renal dysplasia	
Grade II hydronephrosis	
P yeloureteral stenosis	
Physical deformities	4/414 (0.9%)
Bilateral equinus foot deformity	
Syndactyly	
Bilateral supernumerary appendices	
Angioma	
Chromosomal disorder	2/414 (0.4%)
Gastrointestinal	1/414 (0.2%)
Anal atresia	
Other	
Laryngomalacia	1/414 (0.2%)
Presacral cystic teratoma	1/414 (0.2%)

ALSA, aberrant left subclavian artery; ARSA, aberrant right subclavian artery; HIV, human immunodeficiency virus; VSD, ventricular septal defect.

356/402 (89.3%) had a PVL of less than 50 copies/mL and a median CD4 count of 630 cells/mL (IQR, 415–859). There were 24/402 (5.9%) women with detectable PVLs between 50 and 500 copies/mL and 22/402 (5.4%) with PVLs greater than 1000 copies/mL. Among the children of the 46 pregnant women with PVLs greater than 50 copies/mL, there were 3 cases of VT, corresponding to a rate of 6.5% (95% confidence interval [CI] 0%–13.66%).

As regards the characteristics of the offspring, 230/388 (59.3%) were born via vaginal delivery. Among those born by caesarean section (158/388; 40.7%) 51/388 (13.1%) were born by emergency caesarean section. The sex distribution was fairly uniform (52% female vs 48% male). The proportion of preterm birth was 11.1% (46/414), and only 12/414 (2.9%) were born before 32 weeks' gestation. There were 40/414 infants with low birth weight for gestational age, and a total of 18 congenital anomalies were identified in the cohort (Tables 3 and 4).

The most frequently used neonatal prophylaxis regimen (in 358/414 [86.5%]) was monotherapy with azidothymidine (AZT) for 4 weeks. A total of 45/414 infants (10.9%) received combination therapy with 3 drugs for 4 weeks (AZT, nevirapine [NVP] and lamivudine [3TC]) and 2 infants received an integrase inhibitor (raltegravir). There were 3 cases in which infants did not receive neonatal prophylaxis, none of whom acquired the infection.

There were 3 cases of VT of HIV in the total cohort (0.72%; 95% CI, 0%–1.54%) with a positive PCR test within 48 h of birth. Two pregnant women (one from Spain, one from Guinea) received the diagnosis of HIV infec-

Table 4 Anomalies described in the offspring of mothers living with HIV in Spain.

Pregnant woman				Exposed newborn infant	
Age (years)	Time of HIV diagnosis	ART during pregnancy	Substance use	Gestational age (weeks)	Congenital anomaly
1. Cardiovascular anomaly, n/N (%): 5/18 (27.8)					
36	Before gestation	RAL + TDF/TAF		37	Membranous VSD
27	Before gestation	ABC/3TC + RAL	Tobacco	36	Right aortic arch, ALSA, PLSVC draining in coronary sinus
26	During gestation	TDF/FTC + RAL		38	Left ventricular hypertrophy
35	Before gestation	ABC/3TC/NVP		37	IUGR, right aberrant subclavian artery
38	Before gestation	ABC/3TC + DRV/COBI (switched to ABC/3TC + RAL)		30	Patent foramen ovale
2. Renal anomaly, n/N (%): 4/18 (22.2)					
25	Before gestation	TAF/FTC/EVG/COBI (switch to AZT/3TC/RAL)		39	Left pyeloureteral stenosis
37	Before gestation	ABC/3TC/DTG (cambia a TDF/FTC + RAL)		41	Right-sided grade II hydronephrosis
39	Before gestation	TDF/FTC + RAL		32	Left horseshoe kidney
30	Before gestation	TAF/FTC/RPV		39	Dysplasia of right kidney with cavum vergae
3. Physical deformity, n/N (%): 4/18 (22.2)					
27	During gestation	TDF/FTC + RAL		38	Bilateral equinus foot + syndactyly + agenesis + facial paralysis (Smith-Lemli-Opitz syndrome)
31	Before gestation	No data		40	Syndactyly + hypertelorism + anonychia of third right finger + left-sided cryptorchidism + bilateral optic nerve hypoplasia
41	Before gestation	TAF/FTC/BIC (cambia a ABC/3TC + RAL)	Alcohol	40	Bilateral supernumerary appendices 5th finger of both hands
34	Before gestation	TDF/FTC + RAL	Tobacco	35	Angioma
4. Chromosomal disorder, n/N (%): 2/18 (11.1)					
41	Before gestation	TDF/FTC + DRV/COBI		37	Trisomy 21
41	Before gestation	ABC/3TC/DTG		36	Chromosomal disorder
5. Gastrointestinal anomaly, n/N (%): 1/18 (5.5)					
23	Before gestation	No data		37	Anal atresia
6. Other					
37	Before gestation	ABC/3TC + RAL		38	Presacral cystic teratoma
35	Before gestation	TDF/FTC + DTG		37	Laryngomalacia

ABC, abacavir; ALSA, aberrant left subclavian artery; ART, antiretroviral therapy; AZT, azidothymidine; BIC, bictegravir; COBI, cobicistat; DTG, dolutegravir; DRV, darunavir; EVG, elvitegravir; FTC, emtricitabine; HIV, human immunodeficiency virus; IUGR, intrauterine growth restriction; NVP, nevirapine; PLSVC, persistent left superior vena cava; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir; VSD, ventricular septal defect; 3TC, lamivudine.

tion in the third trimester (at week 35 and week 36 of gestation). The former had a negative serologic test result in the second trimester, when she started prenatal care, and probably underwent primary infection during that trimester, with the diagnosis confirmed on week 35. Both received ART with tenofovir/emtricitabine/raltegravir (TDF/FTC/RAL) and had a detectable PVL at the time of childbirth (18 849 and 273 copies/mL, respectively). The third case of VT also involved a woman from Guinea who received the diagnosis on week 28 upon arriving to Spain and starting prenatal care. Although she started treatment with tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV), her adherence was poor, and she also had a detectable PVL at the time of childbirth (95.000 copies/mL). All 3 women gave birth via planned caesarean section on week 38. The infants, with adequate weight for gestational age, received triple combination therapy with AZT + NVP + 3TC, and the diagnosis of HIV was confirmed with a second positive PCR test on days 4, 7 and 14 post birth, respectively.

There were no detected cases of VT of HBV or HCV. There was one case of VT of syphilis (0.24%; 95% CI, −0.23 to 0.71%).

As regards infant nutrition, all infants were formula fed. There was only one infant who was breastfed for one week. Infection by HIV was ruled out in this case.

Discussion

At present, in Spain, pregnant women living with HIV tend to be immigrants, be diagnosed before gestation, have good virologic control and give birth to healthy children.

The HIV vertical transmission rate in countries in Western Europe has decreased sharply in the past few years.[1,2] As observed in previous cohorts in Spain followed up for long periods,[7,8] we have witnessed important epidemiological changes in women living with HIV in recent decades, finding that a majority of infected pregnant women are immigrants. In many instances, these women are particularly vulnerable, as they experience considerable stigma in their countries of origin as well as difficulty accessing the health care system in Spain, which can delay initiation of prenatal care or ART during pregnancy.

Similarly, while current data show that, following sexual transmission, the most frequent route of transmission of HIV is intravenous drug use,[9] we ought to highlight the proportion of women in our cohort who acquired the infection via VT that have reached adulthood and have now become mothers. It should be taken into account that these patients have a previous history of exposure to multiple ART regimens, which entails the possibility of drug resistances, and in some cases their immune status may be worse compared to women who have been infected for shorter periods.[10]

At present, there are treatments available for situations where there is a high risk of VT, such as late diagnosis during pregnancy or poor adherence to ART. Integrase inhibitors (INIs), considered the first-line treatment for adults in current guidelines,[11,12] are very useful in these situations due to their adequate transplacental transfer and their ability to decrease the maternal PVL in a relatively short period.[13,14] In adherence to recommendations issued in recent years, the data for our cohort show that the most currently prescribed regimen at present is the combination of 2 nucleoside analogues and one INI (chiefly raltegravir).

Concerning the reasons for switching the ART regimen during pregnancy, in our analysis, more than 80% of modifications were made to prevent the potential toxicity of the regimen, in adherence to the latest guidelines on VT prevention that propose first-line regimens based on effectiveness and safety data,[11,12] since this is a special situation in which the potential adverse effects on both mother and child must be taken into account.[12]

When it came to the modality of delivery chosen for women living with HIV, advances in ART and the adequate viral suppression that is usually achieved in these patients, in addition to the improved knowledge of the main risk factors associated with VT, allowed a less invasive approach in obstetric care. For a few years now, elective caesarean section has been reserved for patients who do not achieve an undetectable PVL in the third trimester or who were diagnosed late.[12,15] The data obtained in our cohort reflect this situation, as planned caesarean delivery was implemented in fewer than a third of cases (27.6%), a proportion that was substantially smaller compared to the proportion observed in the Madrid cohort in previous years (53% in the 2000–2006 period and 42.8% in the 2007–2013 period).[7] In addition, this proportion may have been overestimated, as the reason for the intervention was not documented, and there may have been cases in which the indication for caesarean delivery was purely obstetric and unrelated to HIV.

Neonatal prophylaxis, another cornerstone of VT prevention, has been evolving over time in terms of the composition and duration of the regimen.[12,15–17] After classifying the infant based on the risk of acquiring the infection, the optimal regimen is selected on a case-by-case basis in adherence with current guidelines.[12] Due to the large percentage of mothers who received adequate prenatal care and HIV suppression and immune status in the cohort, monotherapy with AZT was the prophylaxis strategy selected in 85% of infants. We ought to highlight that 3 infants received no prophylaxis, a strategy currently contemplated in some countries, such as Switzerland, in newborn infants considered to be at very low risk.[18] Although none of them became HIV positive, current guidelines in Spain do not contemplate this approach under any circumstances,[12] and while shorter courses are recommended for infants at lower risk, prophylaxis should be initiated within hours from birth. The 10.9% of neonates who received a combination of three drugs for prophylaxis were infants at high risk of VT (chiefly whose mothers had a detectable PVL at the time of delivery), which reflects that this is a preventive strategy that is widely applied in this scenario. Although there is no evidence of the benefits of a three- versus a two-drug regimen, the rationale for using the former is the importance of achieving maximum suppression of viral replication early on in the case of infection, and by extrapolation of guidelines for postexposure prophylaxis in adults, which, for cases with a lower risk of transmission compared to VT, recommend a three-drug regimen. This early suppression could limit the establishment of HIV reservoirs, potentially enabling ART-free remission, as suggested by recent findings in a small sample of very-high risk infected infants.[19]

As regards the observed prevalence of congenital anomalies(18/414; 4.3%) we ought to highlight that it was 5

times the prevalence reported in the general population in Spain (0.86% in year 2021),[20] however, this difference was lesser compared to the prevalence in the latest report of the Antiretroviral Pregnancy Registry (2.9%; 95% CI, 2.7–3.2).[21] After an initial warning of a potential association between exposure to dolutegravir around conception and an increased incidence of neural tube defects,[22] in recent years a growing body of data from different studies has not supported this association,[23–25] so dolutegravir is currently the first-line drug also during pregnancy. Therefore, after avoiding the use of this drug during the initial period of uncertainty, as reflected in the presented data, at present dolutegravir is included in the regimens commonly used in pregnant women, even when ART is initiated during pregnancy.

The proportion of congenital anomalies could be associated with increased detection secondary to the specific documentation of these diseases in the register, but the sample size precluded drawing firm conclusions, so active surveillance must be maintained and our findings combined with those of other European cohorts to elucidate these aspects and identify the potential adverse effects of novel antiretroviral drugs.

In recent years, evidence showing that ''undetectable'' is tantamount to ''intransmissible'' via sexual contact as long as the affected individual continues to receive ART and remains under monitoring[26] has prompted consideration whether it would be possible to extrapolate this statement to breastfeeding (BF) in infants born to mothers with adequately controlled HIV infection. The widespread dissemination of the multiple benefits to infants associated with this feeding modality has led some women to express a desire to breastfeed.

The most robust data on BF derive from the PROMISE study, which showed that the risk of transmission through human milk in mothers with ART and an undetectable viral load during pregnancy and in the postpartum period who breastfed was lower than 1%, but not 0%.[27] However, this study was conducted in low-income countries, where adherence was not strict in cases of infection, in which mothers had a detectable PVL at the time the infant acquired the infection. On the other hand, recent data from European groups show VT rates associated to BF of 0 in the case of mothers with good adherence to ART, a suppressed PVL and receiving regular clinical care,[28] so a debate is underway regarding the benefits of BF and the right of the mother to breastfeed in relation to the risk of potential infection in the infant.[12,16,29]

We must underscore the importance of establishing programmes to fund formula feeding in the first year of life for these patients. In our cohort, there was one case in which the mother covertly breastfed for a few days due to social pressure, which highlights the crucial role of the paediatrician in discussing infant feeding with the mother to try to avoid the stigma associated with the recommendation of adapted formula feeding. In cases where the maternal viral load has been undetectable during pregnancy and continues to be undetectable in the postpartum period, it would be possible to develop, if the mother wishes to breastfeed, a specific follow-up plan. In the only case of BF identified in our cohort, the infant had been born to a mother with an undetectable PVL and good adherence to ART. However, if the mother has not maintained an undetectable viral load or has started ART recently, the option of supporting BF is more difficult and involves far greater risks.

Lastly, we ought to highlight that there are still cases of VT of HIV in Spain, in most instances due to missed opportunities, frequently with late initiation of ART and failure to achieve an undetectable viral load by childbirth, as occurred in three neonates in the cohort. In all three, VT occurred in utero, and the infection became established despite immediate initiation of postexposure prophylaxis after birth with a three-drug regimen. The risk factors that are relevant in the current population, such as immigrant status, should be taken into account in order to reinforce the preventive measures that are within our reach, in addition to assessing adherence to ART at regular intervals during pregnancy, with proposed strategies including directly observed therapy in patients with risk factors for poor adherence.

Among the limitations of our study, we ought to mention the loss of information that would have been relevant for some of the analyses due to the data collection method and the lack of participation of some autonomous communities in Spain. In a high percentage of cases, the route of HIV transmission to the mother had not been documented, although this absence suggests that HIV was probably transmitted through sexual contact. Notwithstanding, this cohort is the broadest in terms of the coverage of the national territory, offering a global perspective of the characteristics of pregnant women living with HIV and their offspring and allowing an assessment of the current situation and temporal trends in VT in Spain as well as surveillance of the potential adverse events associated with ART.

Conclusion

At present, most women living with HIV in Spain are immigrants and receive ART during gestation, which achieves an adequate immune status and virologic control at the time of childbirth, and their exposed newborn infants become healthy children.

Although the VT rate of HIV in Spain is very low (0.72%), the goal continues to be its total eradication. To this end, it is crucial that preventive measures are reinforced, using the tools at our disposal to achieve an undetectable PVL at the time of delivery. In addition, exposed infants must receive prophylaxis based on the risk of infection and be closely followed up to rule out infection by HIV and other possible infections and to monitor for potential adverse effects of exposure to ART.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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